

Form PTO-1449

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
60390-G/JPW/GJG/JBCSerial No.  
09/728,616

Applicants: Arlindo L. Castelhan , et al.

Filing Date  
December 1, 2000

Group

INFORMATION DISCLOSURE CITATION  
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## U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	5 2 9 6 4 8 4	3/22/94	Coghlan, M. J. et al. (Exhibit 1);			
	5 4 0 9 9 3 0	4/25/95	Spada, A. P. et al. (Exhibit 2);			
	5 5 1 6 8 9 4	5/14/96	Reppert S. M. (Exhibit 3);			
	5 5 8 0 8 7 0	12/3/96	Barker, A. J. et al. (Exhibit 4);			
	5 6 4 6 1 3 0	7/8/97	Shi, G. H. (Exhibit 5);			
	5 6 8 1 9 4 1	10/28/97	Cook, P. D. et al. (Exhibit 6);			
	5 7 1 0 1 5 8	1/20/98	Myers, M. R. et al. (Exhibit 7);			
	5 7 1 4 4 9 3	2/3/98	Myers, M. R. et al. (Exhibit 8);			
	5 7 2 1 2 3 7	2/24/98	Myers, M. R. et al. (Exhibit 9);			
	5 7 4 7 4 9 8	5/5/98	Schnur, R.C. et al. (Exhibit 10);			
	5 7 8 0 4 5 0	7/14/98	Shade, D. L. (Exhibit 11);			
	5 9 6 2 4 5 8	10/5/99	Lohmann, et al. (Exhibit 12);			

## FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation
					Yes No
WO 9 4 1 7 0 9 0	8/4/94	PCT (Exhibit 13);			
WO 9 5 1 1 6 8 1	5/4/95	PCT (Exhibit 14);			
WO 9 5 2 0 5 9 7	8/3/95	PCT (Exhibit 15);			

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)


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Applicants: Arlindo L. Castelhan, et al.  
Serial No.: 09/728,616  
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Exhibit A

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	WO 9 6 1 9 4 7 8	6/27/96	PCT (Exhibit 16);				
	WO 9 7 0 5 1 3 8	2/13/97	PCT (Exhibit 17);				
	WO 9 7 3 3 8 7 9	9/18/97	PCT (Exhibit 18);				
	WO 9 8 0 8 3 8 2	3/5/98	PCT (Exhibit 19);				
	WO 9 8 2 2 4 6 5	5/28/98	PCT (Exhibit 20);				
	WO 9 9 0 6 0 5 3	2/11/99	PCT (Exhibit 21);				
	WO 9 9 0 8 4 6 0	2/18/99	PCT (Exhibit 22);				
	WO 9 9 3 3 8 1 5	7/8/99	PCT (Exhibit 23);				
	WO 9 9 4 2 0 9 3	8/26/99	PCT (Exhibit 24);				
	EP 0 3 2 2 2 4 2	6/28/89	EPO (Exhibit 25);				
	EP 0 7 2 9 7 5 8	4/9/96	EPO (Exhibit 26);				
	JP 9 2 9 1 0 8 9	5/11/99	Japan (Abstract Only) (Exhibit 27);				

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Blazynski C., (1990) "Discrete Distributions of Adenosine Receptors in Mammalian Retina", <u>Journal of Neurochemistry</u> , 53: 648-655 (Exhibit 28);
	Braas K.M., et al., (1987) "Endogenous adenosine and adenosine receptors localized to ganglion cells of the retina", <u>Proceedings of the National Academy of Science</u> , 84: 3906-3910 (Exhibit 29);
	Bradford M. M., (1976) "A Rapid and Sensitive Method for the Quantitation of Microgram Quantities of Protein Utilizing the Principle of Protein-Dye Binding", <u>Anal. Biochem.</u> , 72: 248-254 (Exhibit 30);

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	Feoktistove, I. et al., (1998) "Adenosine A <sub>2B</sub> receptors: a novel therapeutic target in asthma?", <u>TIPS</u> 19: 148-153 (Exhibit 36);
	GenBank accession numbers S45235 and S56143 (Exhibit 37);
	GenBank accession # S46950 (Exhibit 38);
	Kang, Y. et al., (1990) "Effects of Expression of Mammalian G $\alpha$ and Hybrid Mammalian-Yeast G $\alpha$ Proteins on the Yeast Pheromone Response Signal Transduction Pathway", <u>Mol. Cell. Biol.</u> , 10: 2582-2590 (Exhibit 39);
	Muller, C. E. and Stein, B. (1996) "Adenosine Receptor Antagonist: Structure and Potential Therapeutic Applications", <u>Current Pharmaceutical Design</u> , 2: 501-530 (Exhibit 40);
	Muller, C. E. (1997) "A <sub>1</sub> -Adenosine Receptor Antagonists", <u>Exp. Opin. Ther. Patents</u> 7(5): 419-440 (Exhibit 41);
	Muller, C. E., et al., (1997) "Synthesis and Structure-Activity Relationships of 3,7-Dimethyl-1-propargylxanthine Derivatives, A <sub>2A</sub> -Selective Adenosine Receptor Antagonists", <u>J. Med. Chem.</u> , 40: 4396-4405 (Exhibit 42);

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## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Nyce J. W. and Metzger J.W., (1997) "DNA antisense therapy for asthma in an animal model", <u>Nature</u> , 385: 721-725 (Exhibit 43);
	Pichler, H. et al. (1986) "Synthese of 7-unsubstituierten 7H-Pyrrolo[2,3-d] pyrimidines", <u>Liebigs Ann. Chemie.</u> , 9: 1485-1505 (Exhibit 44);
	Seela, F., and Lupke, U., (1977) <u>U. Chem. Ber.</u> , 110:1462-1469 (Exhibit 45);
	Strohmeier, G. R. et al., (1995) "The A <sub>2b</sub> Adenosine Receptor Mediates cAMP Responses to Adenosine Receptor Agonists in Human Intestinal Epithelia", <u>J. Bio. Chem.</u> , 270: 2387-2394 (Exhibit 46);
	Williams, E. F. et al., (1994) "Nucleoside transport sites in a cultured human retinal cell line established by SV-40 T antigen gene", <u>Current Eye Research</u> , 13: 109-118 (Exhibit 47);
	Woods, C. L. and Blazynski, C. (1991) "Characterization of Adenosine A <sub>1</sub> -receptor Binding Sites in Bovine Retinal Membranes", <u>Experimental Eye Research</u> , 53: 325-331 (Exhibit 48);

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	5 6 3 9 9 1 3	6/17/97	Lidor, R. et al. (Exhibit 50);			
	5 8 3 4 6 0 9	11/10/98	Horne, D. A. et al. (Exhibit 51);			
	5 8 7 7 2 1 8	3/2/99	Herzig, Y. et al. (Exhibit 52);			
	5 8 7 7 2 2 1	3/2/99	Cohen, S. et al. (Exhibit 53);			
	5 8 8 0 1 5 9	3/9/99	Herzig, Y. et al. (Exhibit 54);			
	5 9 1 4 3 4 9	6/22/99	Cohen, S. et al. (Exhibit 55);			
	5 9 9 4 4 0 8	11/30/99	Cohen, S. et al. (Exhibit 56);			
	6 1 0 3 8 9 9	8/15/00	Horne, D. A. et al. (Exhibit 57);			

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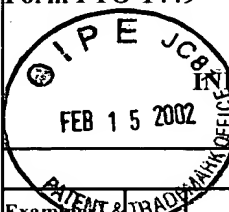
	Document Number	Date	Country	Class	Subclass	Translation	
						Yes	No
	WO 9 9 6 2 5 1 8	12/9/99	PCT (Exhibit 49);				
	WO 9 4 2 4 1 3 6	10/27/94	PCT (Exhibit 58);				
	WO 9 5 1 8 6 1 7	7/13/95	PCT (Exhibit 59).				

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)


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Examiner's Initial	Document Number			Date	Name	Class	Subclass	Filing Date if Appropriate
	3 0 3 7 9 8 0			6/5/62	Hitchings, G. H. et al. (Exhibit 60);			
<b>FOREIGN PATENT DOCUMENTS</b>								
	Document Number			Date	Country	Class	Subclass	Translation Yes No
	WO	9	3 2 0 0 7 8	10/14/93	PCT (Exhibit 61);			
	WO	9	4 1 3 6 7 6	6/23/94	PCT (Exhibit 62);			
	WO	9	5 1 9 9 7 0	7/27/95	PCT (Exhibit 63);			
	WO	9	8 0 7 7 2 6	2/26/98	PCT (Exhibit 64);			
	WO	9	8 5 7 6 5 1	12/23/98	PCT (Exhibit 65);			
	EP	0	5 1 4 5 4 0	11/25/92	EPO (Exhibit 66);			
	EP	0	6 8 2 0 2 7	11/15/95	EPO (Exhibit 67);			
	EP	0	7 2 9 7 5 8	9/4/96	EPO (Exhibit 68);			
	EP	0	7 7 3 0 2 3	5/14/97	EPO (Exhibit 69);			
	GB	9	1 5 3 0 3	1/9/63	GB (Exhibit 70);			
	DE	3	1 4 5 2 8 7	5/19/83	DE (Exhibit 71);			
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>								
	Iwamura, H. et al. (1996) "Quantitative Aspects of the Receptor Binding of Cytokinin Agonists and Antagonists" <u>J. Med. Chem.</u> , 26: 838-844 (Exhibit 72);							
	Jorgensen, A. et al. (1985) "Synthesis of 7H-Pyrrolo[2,3-d]pyrimidin-4-amines" <u>Liebigs, Ann. Chem.</u> , Pages 142-148 (Exhibit 73);							
	Kiichiro, K. et al. "Synthesis of pyrazinecarboxylic acid derivs. - (II) derivs. of 3-aminopyrazinecarboxylic acid" (Abstract only) (Exhibit 74);							
	Muller, E. C. et al. (1996) "Chiral Pyrrolo[2,3-d]pyrimidine and Pyrimido[4,5,-b]indole Derivatives: Structure-Activity Relationships of Potent, Highly Stereoselective A <sub>1</sub> -Adenosine Receptor Antagonist" <u>J. Med. Chem.</u> , 39: 2482-2491 (Exhibit 75);							
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## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Muller, C. E. et al. (1990) "7-Deaza-2-phenyladenines: Structure-Activity Relationships of Potent A1 Selective Adenosine Receptor Antagonists" <u>J. Med. Chem.</u> , 33: 2822-2828 ( <b>Exhibit 76</b> );
	Venugopalan, B. et al. (1998) "Synthesis of 6,7-Dimethoxypyrimido[4,5-b]-indoles as Potential Antihypertensive Agents" <u>J. Heterocyclic Chem.</u> , 25: 1633-1639 ( <b>Exhibit 77</b> ); and
	West, R. A. et al. (1961) "2-Alkyl(aryl)-and 2,7-Dimethyl-4-substituted Aminopyrrolo[2,3-d]pyrimidines" <u>J. Org. Chem.</u> , 26: 3809-3810 ( <b>Exhibit 78</b> );
	DeNinno, M.P. in <u>Annual Reports in Medicinal Chemistry</u> , Vol. 33, (Academic Press: San Diego, 1998), pp. 111-120 ( <b>Exhibit 79</b> );
	Hart, H. et al., <u>Organic Chemistry, A Short Course</u> , (Houghton Mifflin: 1995), p. 121 ( <b>Exhibit 80</b> );

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	5 6 4 6 1 5 6	7/8/97	Jacobson, et al. (Exhibit 81);			
	5 7 8 0 4 8 1	7/14/98	Jacobson, et al. (Exhibit 82);			
	3 9 1 0 9 1 3	10/7/75	Kim, et al. (Exhibit 83)			

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					Yes	No
WO 0 0 0 3 7 4 1	1/27/00	PCT (Exhibit 84);				

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Abbracchio M., et al., (1999) "Brain Adenosine Receptors as Targets for Therapeutic Intervention in Neurodegenerative Diseases", <u>Ann. NY. Acad. Sci.</u> , 890: 79-92 (Exhibit 85);
	Abbracchio M., et al., (1997) "Modulation of Apoptosis by Nervous System: a Possible Role for the A <sub>3</sub> Receptor", <u>Ann. NY. Acad. Sci.</u> , 825: 11-22 (Exhibit 86);
	Baraldi P., et al., (2000) "New potent and selective human adenosine A <sub>3</sub> receptor antagonists", <u>Tips</u> , 21: 456-459 (Exhibit 87);
	Brand A., et al., (2001) "Adenosine A1 and A3 receptors mediate inhibition of synaptic transmission in rat cortical neurons", <u>Neuropharmacology</u> , 40: 85-95 (Exhibit 88);
	Casavola V., et al., (1998) "Adenosine A3 receptor activation increases cystolic calcium concentration via calcium influx in A6 cells", <u>Drug Development Research</u> , 43 (1): 62 (Exhibit 89)

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	Ezeamuzie C., et al., (1999) "Adenosine A3 receptors on human eosinophils mediate inhibition of degranulation and superoxide anion release", <u>British Journal of Pharmacology</u> , 127: 188-194 ( <b>Exhibit 90</b> );	
	Fozard J., et al., (1996) "Mast cell degranulation following adenosine A3 receptor activation in rats", <u>European Journal of Pharmacology</u> , 298: 293-297 ( <b>Exhibit 91</b> );	
	Franco M., et al., (1999) "Adenosine Regulates Renal Nitric Oxide Production in Hypothyroid Rats", <u>Journal of the American Society of Nephrology</u> , 1681-1688 ( <b>Exhibit 92</b> );	
	Guerra L., et al., (1998) "Adenosine A3 receptor activation increases cytosolic calcium influx in A6 cells", <u>Nephrology Dialysis Transplantation</u> , 13 (6): A5 ( <b>Exhibit 93</b> );	
	Jacobson K.A., et al., (1998) "Adenosine A3 receptors: novel ligands and paradoxical effects", <u>Tips</u> , 19:184-191 ( <b>Exhibit 94</b> );	
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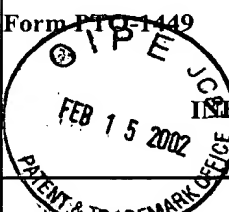
## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Jacobson K.A., et al., (1997) "Pharmacological Characterization of Novel A3 Adenosine Receptor-selective Antagonists", <u>Neuropharmacology</u> , 36 (9): 1157-1165 ( <b>Exhibit 95</b> );
	Lee T., et al., (2000) "Protective effects of renal ischemic preconditioning and adenosine pretreatment: role of A1 and A3 receptors", <u>Am. J. Physiol. Renal Physiol.</u> , 278: F380-F387 ( <b>Exhibit 96</b> );
	Ohana G., et al., (2001) "Differential Effect of Adenosine on Tumor and Normal Cell Growth: Focus on the A3 Adenosine Receptor", <u>Journal of Cellular Physiology</u> , 186: 19-23 ( <b>Exhibit 97</b> );
	Regulation of Downstream Effectors By GPCRs, (1999) <u>FASEB J.</u> , Abstracts 147.1-147.6 ( <b>Exhibit 98</b> );
	Reshkin J., et al., (2000) "Activation of A3 Adenosine Receptor Induces Calcium Entry and Chloride Secretion in A6 Cells", <u>J. Membrane Biol.</u> , 178: 103-113 ( <b>Exhibit 99</b> );
	Sawynok J., et al., (1997) "Adenosine A3 receptor activation produces nociceptive behaviour and edema by release of histamine and 5-hydroxytryptamine", <u>European Journal of Pharmacology</u> , 333: 1-7 ( <b>Exhibit 100</b> );

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		Von Lubitz, D., et al., (1999) "Chronic administration of adenosine A3 receptor agonist and cerebral ischemia: neuronal and glial effects", <u>European Journal of Pharmacology</u> , 367: 157-163 ( <b>Exhibit 101</b> );					
		Von Lubitz D., et al., (1999) "Stimulation of Adenosine A3 Receptors in Cerebral Ischemia", <u>Ann. NY. Acad. Sci.</u> , 890: 93-106 ( <b>Exhibit 102</b> );					
		Yao Y., et al., (1997) "Adenosine A3 Receptor Agonists Protect HL-60 and U-937 Cells from Apoptosis Induced by A3 Antagonists", <u>Biochemical And Biophysical Research Communications</u> , 232: 317-322 ( <b>Exhibit 103</b> ); and					
		Zhao Z., et al., (2000) "A rôle for the A3 Adenosine receptor in determining tissue levels of cAMP and blood pressure: studies in knock-out mice", <u>Biochimica et Biophysica Acta</u> , 1500: 280-290 ( <b>Exhibit 104</b> )					
		International Search Report for International Application No. PCT/US99/12135 ( <b>Exhibit 105</b> );					
		International Search Report for International Application No. PCT/US00/32702 ( <b>Exhibit 106</b> );					
		Lee T., et al., (1999) "Protective effects of renal ischemic preconditioning and adenosine pretreatment: role of A1 and A3 receptors", <u>72<sup>nd</sup> Scientific Sessions of the American Heart Association</u> , Atlanta, GA, p.197 ( <b>Exhibit 107</b> );					
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	WO	9	7	0	2	2	6	6	1/23/97	PCT (Exhibit 109);				
	IN	1	5	7	2	8	0		2/22/86	India (Exhibit 110);				

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		Mautner, H.G., (1961) "Potential Deoxyribonucleic Acid Cross-linking Agents. 8,8'-Bisporines", J. Org. Chem. 26(6):1914-1917 (Exhibit 111); and
		PCT International Preliminary Examination Report for International Application No. PCT/US99/12135 (Exhibit 112).

EXAMINER

DATE CONSIDERED

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.